
Diethylene Glycol

CAS #111-46-6

Swiss CD-1 mice, at 0.0, 0.35, 1.75, and 3.5%, drinking water

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Diethylene glycol (DEG), a common chemical and solvent used in industry and in consumer goods, was tested for reproductive toxicity in Swiss CD-1 mice using the RACB protocol (Williams et al., *Fundam Appl Toxicol* 14:622-635 [1990]). It was part of a large structure-activity series of glycol ethers and congeners evaluated using this design. F₀ mice were exposed to drinking water containing 0.0, 0.35, 1.75, and 3.5% DEG. Based on water consumption data collected during the study, these concentrations produced calculated DEG consumptions of approximately 612, 3062, and 6125 mg/kg/day.

While F₀ body weight was unchanged by DEG consumption during the Task 2 mating period, the number of litters per pair was reduced by 12% at the top dose, and the number of live pups per litter was

reduced by 32%. Pup weight adjusted for litter size was reduced by approximately 12% at the top dose level. In a crossover mating to determine the affected sex, number of pups per litter was equivalent across the three groups, but adjusted pup weight was reduced by 10% in the control male × 3.5% DEG female mating. After the F₁ mice were weaned, the control and 3.5% DEG F₀ mice were killed and necropsied. There were no treatment-related changes in male organ weights or histopathology, while female body weight was reduced by 7% after 3.5% DEG consumption. Adjusted organ weights were unchanged.

For the F₁ mating trial, exposed mice from the 1.75% group were used, because insufficient mice were available from the top dose, due to reduced fertility in that group. DEG at 1.75% did not affect pup

survival to mating at postnatal day 74. There were no treatment-related alterations in the number or weight of F₂ pups in the Task 4 mating trial. After all the F₂ litters were born and the F₁ females subjected to estrous cyclicity evaluation, the F₁ mice were killed and necropsied. There was an 11 and 7% decrease in the body weights of the treated males and females, respectively. No organ weights were affected nor were sperm indices changed.

In summary, diethylene glycol at 3.5% was a reproductive toxicant in Swiss CD-1 mice, based on reductions in litters per pair, and in mean litter size. In F₀ mice, this was unaccompanied by body weight loss, while in F₁ mice, there was reduced body weight in the absence of a fertility effect.

Summary: NTP Reproductive Assessment by Continuous Breeding Study.

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Chemical: Diethylene Glycol

CAS#: 111-46-6

Mode of exposure: Drinking water

Species/strain: Swiss CD-1 mice

F ₀ generation	Dose concentration →	0.35%	1.75%	3.5%
General toxicity		Male, female	Male, female	Male, female
Body weight		—, —	—, —	—, ↓
Kidney weight ^a		•, •	•, •	•, •
Liver weight ^a		—, —	—, —	—, —
Mortality		•, •	•, •	•, •
Feed consumption		•, •	•, •	•, •
Water consumption		•, •	•, •	•, •
Clinical signs		•, •	•, •	•, •

Reproductive toxicity			
̄ litters/pair	—	—	↓
# live pups/litter; pup wt./litter	—, —	—, —	↓, ↓
Cumulative days to litter	—	—	—
Absolute testis, epididymis weight ^a	•	•	—, —
Sex accessory gland weight ^a (prostate, seminal vesicle)	•	•	—, —
Epidid. sperm parameters (#, motility, morphology)	•	•	—, —, —
Estrous cycle length	•	•	•

Determination of affected sex (crossover)	Male	Female	Both
Dose level	—	3.5%	—

F ₁ generation	Dose concentration →	•	1.75%	•
General toxicity		Male, female	Male, female	Male, female
Pup growth to weaning		•	•	•
Mortality		•	•	•
Adult body weight		•	↓, ↓	•
Kidney weight ^a		•	•	•
Liver weight ^a		•	—, —	•
Feed consumption		•	•	•
Water consumption		•	•	•
Clinical signs		•	•	•

Reproductive toxicity			
Fertility index	•	—	•
# live pups/litter; pup wt./litter	•	—, —	•
Absolute testis, epididymis weight ^a	•	—, —	•
Sex accessory gland weight ^a (prostate, seminal vesicle)	•	—, —	•
Epidid. sperm parameters (#, motility, morphology)	•	—, —, —	•
Estrous cycle length	•	•	•

Summary information	
Affected sex?	Unclear
Study confounders:	None
NOAEL reproductive toxicity:	1.75%
NOAEL general toxicity:	0.35%
F ₁ more sensitive than F ₀ ?	Yes
Postnatal toxicity:	No

Legend: —, no change; •, no observation; ↑ or ↓, statistically significant change (p<0.05); —, —, no change in males or females. ^aAdjusted for body weight.